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      FILE 'HCAPLUS' ENTERED AT 14:56:34 ON 04 MAY 2004
L1         48134 S ION CHANNEL?
L2           877 S ION (4W) CHANNEL? (4W) MODULAT?
L3             3 S L2 AND RESPIRAT? (4W) DISEAS?
L4           187 S L2 AND REVIEW/DT
L5             1 S L3 AND REVIEW/DT
L6         35009 S L2 OR CYSTIC FIBROSIS OR ASTHMA OR RHINORRHEA OR BLADDER SPAS
L7             1 S ION () (INHIBITOR?) AND (ASTHMA OR CYSTIC () FIBROSIS OR CHRO
L8             0 S L7 AND REVIEW/DT
L9         51158 S ION (3W) CHANNEL?
L10         2187 S L9 AND (CYSTIC () FIBROSIS OR RHINORRHEA? OR MIGRAINE? OR XER
L11          537 S L10 AND REVIEW/DT
L12            0 S L11 AND SKC
L13            0 S L11 AND BKC
L14            0 S L11 AND BIG (4W) CONDUCTANC?
L15            2 S L11 AND INTERM? (4W) CONDUCT?
L16            0 S L11 AND SMALL (5W) CONDUCT?
L17            2 S L11 AND INTERMED? (4W) CONDUCT?
L18            0 S L11 AND BIG (4W) CONDUCT?
L19            0 S L11 AND DUPLICATE REMOVE
L20          535 S L11 NOT L17
L21           84 S L11 AND THERAPEUT?

=> s l20 and ion channels?
       1045967 ION
        660259 IONS
       1391593 ION
                 (ION OR IONS)
        131174 CHANNELS?
         10042 ION CHANNELS?
                 (ION(W)CHANNELS?)
L22          175 L20 AND ION CHANNELS?

=> d l22, ibib abs fhitstr, 20-40

L22  ANSWER 20 OF 175  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:          2003:327029  HCAPLUS
DOCUMENT NUMBER:           139:82785
TITLE:                     Modifier genes in cystic fibrosis lung disease
AUTHOR(S):                 Merlo, Christian A.; Boyle, Michael P.
CORPORATE SOURCE:          Div. Pulmonary Critical Care Med., Johns Hopkins Univ.
                           Sch. Med., Baltimore, MD, USA
SOURCE:                    Journal of Laboratory and Clinical Medicine (2003),
                           141(4), 237-241
                           CODEN: JLCMAK; ISSN: 0022-2143
PUBLISHER:                 Mosby, Inc.
DOCUMENT TYPE:             Journal; General Review
LANGUAGE:                  English
AB   A review. Cystic fibrosis (CF) is caused by mutations in the CF
     transmembrane conductance regulator (CFTR) gene and is characterized by
     progressive lung disease with bronchiectasis and pancreatic exocrine
     insufficiency. A broad spectrum of disease severity exists; some
     individuals with CF die early in childhood, whereas others live well into
     adulthood with only mild lung disease. It is now clear that CFTR genotype
     alone does not account for the wide diversity in CF pulmonary phenotype.
     Evidence is accumulating that secondary genetic factors sep. from the CFTR
     locus significantly influence the severity of CF lung disease. The
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drug targeting
AUTHOR(S): Ciechanover, A.
CORPORATE SOURCE: The Bruce Rappaport Faculty of Medicine and the Rappaport Family Institute for Research in the Medical Sciences, Department of Biochemistry, Technion-Israel Institute of Technology, Haifa, 31096, Israel
SOURCE: Biochemical Society Transactions (2003), 31(2), 474-481
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with refs. Until the early 1980s, protein degrdn. was a neglected research area, and scientists were mostly busy deciphering the genetic code and its translation to the proteome. Destruction of cellular proteins was thought to be a scavenger, non-specific and dead-end process. Although it was known that proteins do turn over, the large extent and high specificity of the process, whereby distinct proteins have half-lives that range from a few minutes to several days, was not appreciated. The discovery of the lysosome by Christian de Duve did not change this view significantly, as it was clear that this organelle is involved mostly in the degrdn. of extracellular proteins, and their proteases cannot be substrate-specific. The discovery of the complex cascade of the ubiquitin pathway revolutionized the field. It is clear now that degrdn. of cellular proteins via the ubiquitin system is a highly complex, temporally controlled and tightly regulated process that plays major roles in a variety of basic pathways and processes during cell life and death, and in health and disease. The system is involved in targeting many cellular proteins, among them cell cycle regulators, growth- and differentiation-controlling factors, transcriptional activators, cell-surface receptors and **ion channels**, endoplasmic reticulum proteins, antigenic proteins destined for presentation on class I MHC mols., and abnormal/misfolded proteins. Consequently, it is involved in regulating many basic cellular processes, such as cell cycle and division, growth and differentiation, signal transduction and transcription, modulation of the secretory and endocytic pathways, the immune and inflammatory responses, and quality control. With the multitude of substrates targeted and the numerous processes involved, it is not surprising that aberrations in the pathway have been implicated in the pathogenesis of many diseases, with certain malignancies and neurodegenerative disorders being ranked among them.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Full Text | Citing References

ACCESSION NUMBER: 2003:249243 HCAPLUS
DOCUMENT NUMBER: 139:174895
TITLE: Peroxynitrite-induced cytotoxicity: mechanism and opportunities for intervention
AUTHOR(S): Virag, Laszlo; Szabo, Eva; Gergely, Pal; Szabo, Csaba
CORPORATE SOURCE: Medical and Health Science Center, Department of Medical Chemistry, University of Debrecen, Debrecen, 4026, Hung.
SOURCE: Toxicology Letters (2003), 140-141, 113-124
CODEN: TOLED5; ISSN: 0378-4274
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Peroxynitrite is formed in biol. systems when superoxide and nitric oxide are produced at near equimolar ratio. Although not a free radical by chem. nature (as it has no unpaired electron), peroxynitrite is a powerful oxidant exhibiting a wide array of tissue damaging effects ranging from lipid peroxidn., inactivation of enzymes and **ion channels** via protein oxidn. and nitration to inhibition of mitochondrial respiration. Low concns. of peroxynitrite trigger apoptotic death, whereas higher concns. induce necrosis with cellular energetics (ATP and NAD) serving as switch between the two modes of cell death. Peroxynitrite also damages DNA and thus triggers the activation of DNA repair systems. A DNA nick sensor enzyme, poly(ADP-ribose) polymerase-1 (PARP-1) also becomes activated upon sensing DNA breakage. Activated PARP-1 cleaves NAD+ into nicotinamide and ADP-ribose and polymerizes the latter on nuclear acceptor proteins. Peroxynitrite-induced overactivation of PARP consumes NAD+ and consequently ATP culminating in cell dysfunction, apoptosis or necrosis. This cellular suicide mechanism has been implicated among others in the pathomechanism of stroke, myocardial ischemia, **diabetes** and **diabetes**-assocd. cardiovascular dysfunction. Here, the authors review the cytotoxic effects (apoptosis and necrosis) of peroxynitrite focusing on the role of accelerated ADP-ribose turnover. Regulatory mechanisms of peroxynitrite-induced cytotoxicity such as antioxidant status, calcium signaling, NFκB activation, protein phosphorylation, cellular adaptation are also discussed.

REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

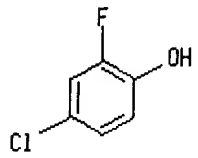
L22 ANSWER 24 OF 175 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:176572 HCAPLUS
DOCUMENT NUMBER: 138:335198
TITLE: The **cystic fibrosis** transmembrane conductance regulator: an intriguing protein with pleiotropic functions
AUTHOR(S): Vankeerberghen, Anne; Cuppens, Harry; Cassiman, Jean-Jacques
CORPORATE SOURCE: Center for Human Genetics, University of Leuven, Louvain, Belg.
SOURCE: Journal of Cystic Fibrosis (2002), 1(1), 13-29
CODEN: JCFOAC; ISSN: 1569-1993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

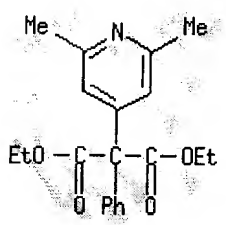
AB A review. **Cystic fibrosis** is a frequent autosomal recessive disorder that is caused by the malfunctioning of a small chloride channel, the **cystic fibrosis** transmembrane conductance regulator. The protein is found in the apical membrane of epithelial cells lining exocrine glands. Absence of this channel results in imbalance of ion concns. across the cell membrane. As a result, fluids secreted through these glands become more viscous and, in the end, ducts become plugged and atrophic. Little is known about the pathways that link the malfunctioning of the CFTR protein with the obsd. clin. phenotype. Moreover, there is no strict correlation between specific CFTR mutations and the CF phenotype. This might be explained by the fact that environmental and addnl. genetic factors may influence the phenotype. The CFTR protein itself is regulated at the maturational level by chaperones and SNARE proteins and at the functional level by several protein kinases. Moreover, CFTR functions also as a regulator of other **ion channels** and of intracellular membrane transport processes. To be able to function as a protein with pleiotropic actions, CFTR seems to be linked with other proteins and with

MF C6 H4 Cl F O
CI COM



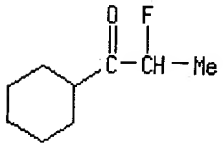
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 157 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Propanedioic acid, (2,6-dimethyl-4-pyridinyl)phenyl-, diethyl ester (9CI)
MF C20 H23 N O4



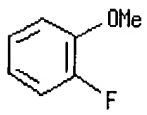
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 157 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 1-Propanone, 1-cyclohexyl-2-fluoro- (8CI, 9CI)
MF C9 H15 F O



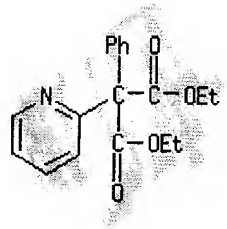
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 157 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Benzene, 1-fluoro-2-methoxy- (9CI)
MF C7 H7 F O
CI COM



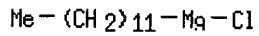
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 157 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Propanedioic acid, phenyl-2-pyridinyl-, diethyl ester (9CI)
MF C18 H19 N O4

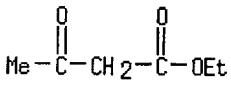


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 157 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Magnesium, chlorododecyl- (8CI, 9CI)
MF C12 H25 Cl Mg



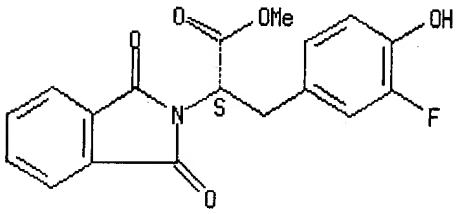
L2 157 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Butanoic acid, 3-oxo-, ethyl ester (9CI)
MF C6 H10 O3
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

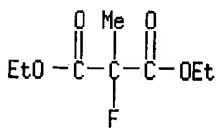
L2 157 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 2H-Isoindole-2-acetic acid, α-[(3-fluoro-4-hydroxyphenyl)methyl]-1,3-dihydro-1,3-dioxo-, methyl ester, (S)- (9CI)
MF C18 H14 F N O5

Absolute stereochemistry.



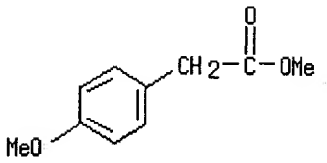
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 157 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Propanedioic acid, fluoromethyl-, diethyl ester (9CI)
MF C8 H13 F O4



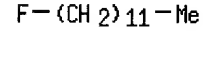
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 157 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Benzeneacetic acid, 4-methoxy-, methyl ester (9CI)
MF C10 H12 O3



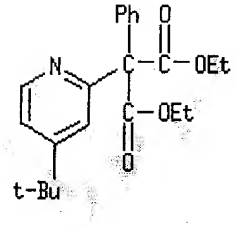
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 157 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Dodecane, 1-fluoro- (6CI, 7CI, 8CI, 9CI)
MF C12 H25 F



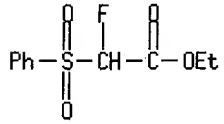
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 157 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Propanedioic acid, [4-(1,1-dimethylethyl)-2-pyridinyl]phenyl-, diethyl ester (9CI)
MF C22 H27 N O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 157 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Acetic acid, fluoro(phenylsulfonyl)-, ethyl ester (8CI, 9CI)
MF C10 H11 F O4 S



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 157 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 1-Naphthalenol, 4-fluoro- (9CI)

Full Text | Citing References

ACCESSION NUMBER: 2004:61248 HCAPLUS
DOCUMENT NUMBER: 140:282500
TITLE: The role of bacterial and non-bacterial toxins in the induction of changes in membrane transport: implications for **diarrhea**
AUTHOR(S): Laohachai, Karina N.; Bahadi, Randa; Hardo, Maria B.; Hardo, Phillip G.; Kourie, Joseph I.
CORPORATE SOURCE: Faculty of Science, Department of Chemistry, Membrane Transport Group, The Australian National University, Canberra, 0200, Australia
SOURCE: Toxicon (2003), 42(7), 687-707
CODEN: TOXIA6; ISSN: 0041-0101
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Bacterial toxins induce changes in membrane transport which underlie the loss of electrolyte homeostasis assocd. with **diarrhea**. Bacterial- and their secreted toxin-types which have been linked with **diarrhea** include: (a) Vibrio cholerae (cholera toxin, El Tor hemolysin and accessory cholera enterotoxin); (b) Escherichia coli (heat stable enterotoxin, heat-labile enterotoxin and colicins); (c) Shigella dysenteriae (shiga-toxin); (d) Clostridium perfringens (C. perfringens enterotoxin, α-toxin, β-toxin and θ-toxin); (e) Clostridium difficile (toxins A and B); (f) Staphylococcus aureus (α-haemolysin); (g) Bacillus cereus (cytotoxin K and haemolysin BL); and (h) Aeromonas hydrophila (aerolysin, heat labile cytotoxins and heat stable cytotoxins). The mechanisms of toxin-induced **diarrhea** include: (a) direct effects on ion transport in intestinal epithelial cells, i.e. direct toxin interaction with intrinsic **ion channels** in the membrane and (b) indirect interaction with ion transport in intestinal epithelial cells mediated by toxin binding to a membrane receptor. These effects consequently cause the release of second messengers, e.g. the release of cAMP/guanosine 3',5'-monophosphate, IP3, Ca2+ and/or changes in second messengers that are the result of toxin-formed Ca2+ and K+ permeable channels, which increase Ca2+ flux and augment changes in Ca2+ homeostasis and cause depolarization of the membrane potential. Consequently, many voltage-dependent ion transport systems, e.g. voltage-dependent Ca2+ influx, are affected. The toxin-formed **ion channels** may act as a pathway for loss of fluid and electrolytes. Although most of the **diarrhea**-causing toxins have been reported to act via cation and anion channel formation, the properties of these channels have not been well studied, and the available biophys. properties that are needed for the characterization of these channels are inadequate.

REFERENCE COUNT: 147 THERE ARE 147 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 537 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:58720 HCAPLUS
DOCUMENT NUMBER: 140:245873
TITLE: Neuronal nicotinic acetylcholine receptor agonists: Pharmacophores, evolutionary QSAR and 3D-QSAR models
AUTHOR(S): Nicolotti, Orazio; Altomare, Cosimo; Pellegrini-calace, Marialuisa; Carotti, Angelo
CORPORATE SOURCE: Dipartimento Farmaco-Chimico, Universita degli Studi di Bari, Bari, 70125, Italy